Ruthenium-catalyzed ring-closing metathesis accelerated by long-range steric effect

AUTHOR(S):

Fujihara, Tetsuaki; Tomike, Yoshikazu; Ohtake, Toshiyuki; Terao, Jun; Tsuji, Yasushi

CITATION:

Fujihara, Tetsuaki ...[et al]. Ruthenium-catalyzed ring-closing metathesis accelerated by long-range steric effect. Chemical communications 2011, 47(34): 9699-9701

ISSUE DATE:

2011-09-14

URL:

http://hdl.handle.net/2433/158313

Journal Name
Dynamic Article Li

Cite this: DOI: 10.1039/c0xx00000x

www.rsc.org/xxxxxx

ARTICLE TYPE

Ruthenium-catalyzed ring-closing metathesis accelerated by long-range steric effect

Tetsuaki Fujihara, Yoshikazu Tomike, Toshiyuki Ohtake, Jun Terao, Yasushi Tsuji*

Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX
DOI: 10.1039/b000000x

Ruthenium-based metathesis catalysts with a *N*-heterocyclic carbene ligand bearing 2,3,4,5-tetraphenylphenyl moieties (1-TPPh and 1-TPPh*) are developed. The highly active catalyst system has been realized in THF by the combination of 1-TPPh* and CuCl as a phosphine scavenger.

Ring-closing metathesis (RCM) is one of the most important synthetic reaction for formation of cyclic compounds containing carbon-carbon double bonds.[1] In the reaction, the Grubbs second-generation catalyst (**1-Me** in Fig. 1)[2a,b] is widely used and shows much higher catalytic activity than the earlier Grubbs first-generation catalyst (**2**: $(PCy_3)_2Cl_2Ru{=}CHPh$).[2b-d] Mechanistic investigations[3] indicate that dissociation[3e] of the tricyclohexylphophine (PCy_3) to the four-coordinate 14-electron species ($LCl_2Ru{=}CHPh$)[3b] is crucial. However, surprisingly, **1-Me** only dissociates PCy_3 less efficiently than **2**.[3c,d] Therefore, in effort to enhance the catalytic activity of **1-Me**, phosphine-free catalysts were prepared by replacing PCy_3 with 3-bromopyridine ligand[4a] or with intramolecular coordination of an isopropoxy substituent of the alkylidene ligand (Hoveyda catalyst: **1-O-Me** in Fig. 1).[4c] However, the 3-bromopyridine catalyst decomposes faster[4b] and **1-O-Me** might be reluctant to dissociate the intramolecular coordination. Furthermore, these alterations and other alkylidene modifications[4d-f] only provide, in principle, the same active catalytic species as from **1-Me** after a single turnover with olefinic substrates. In contrast, variation of the *N*-heterocyclic carbene (NHC) moiety[5] must be capable, since it can directly amend the nature of the 14-electron species to enhance catalytic activity or even realize asymmetric reactions with chiral NHCs.

We recently developed highly active catalyst systems utilizing steric effect at long range (long-range steric effect).[6-8] To exploit such effect, ligands bearing steric bulk apart (> 1 nm) from a coordination cite are requisite. We have already developed very efficient ligands of this nature, i.e., bowl-shaped phosphines[6] and phosphines bearing peripherally arranged oligo(ethylene glycol) chains.[7] Besides them, particularly efficient is 2,3,4,5-tetraphenylphenyl (TPPh) moiety which has rigid and widely spread structure.[8] TPPh moieties provoke steric effect at long range and realize extremely active catalytic activity in Pd-catalyzed air oxidation of alcohol[8a] and kinetic resolution of racemic vinyl ethers.[8b] In the Ru-catalyzed RCM reaction, we anticipate that NHC ligands having TPPh at long range facilitate the phosphine dissociation and shield the resulting 14-electron catalyst species against decompositions[9] such as dimerization (Fig. 2). In this communication, we report synthesis and catalytic activity of Ru catalysts bearing NHC ligands with TPPh and methylated TPPh (TPPh*) substituents (**1-TPPh** and **1-TPPh*** in Fig. 1) in RCM. **1-TPPh** shows much higher catalytic activity than the conventional catalysts such as **1-Me**. Moreover, **1-TPPh*** maintains high catalytic activity even when PCy_3 is scavenged by added CuCl.

1-TPPh was synthesized from 2-bromo-5-iodo-*m*-xylene (See ESI†).[10] Unfortunately, X-ray analysis of **1-TPPh** was not successful. But, the corresponding Hoveyda-type complex (**1-O-TPPh**) derived from **1-TPPh** and 2-isopropoxystyrene[4b] afforded good crystals. The molecular structure of **1-O-TPPh** determined by X-ray structural analysis (Fig. 3) clearly shows that the TPPh moiety on the NHC ligand spatially spreads out and shields the Ru coordination sphere at long-range.‡ The Ru-C (NHC) bond length of **1-O-TPPh** (1.973(5) Å) is quite similar to

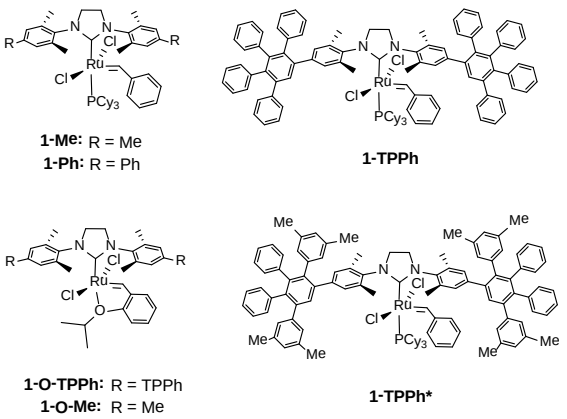


Fig. 1 Structures of catalysts.

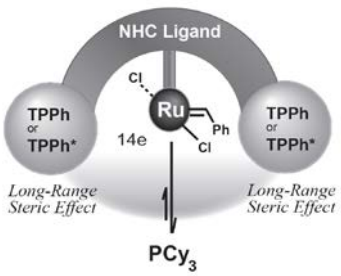


Fig. 2 Ru metathesis catalyst activated by the long-range steric effect

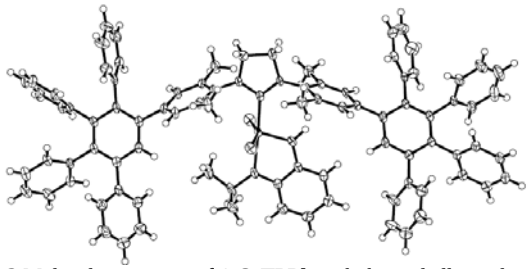
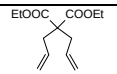
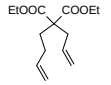
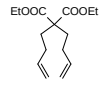
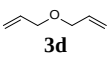


Fig. 3 Molecular structure of **1-O-TPPh** with thermal ellipsoids at 50% probability levels.

Table 1 Ring-closing metathesis of various diolefins.[a]

Entry	Diolefin	Product	Catalyst	Time (h)	Yield (%)[b]
1	 **3a**	 **4a**	**1-TPPh**	17	91 (84)[c]
2			**1-Me**		60
3			**1-Ph**		57
4			**1-O-TPPh**		48
5	 **3b**	 **4b**	**1-TPPh**	8	99 (99)[c]
6			**1-Me**		54
7			**1-Ph**		51
8	 **3c**	 **4c**	**1-TPPh**	6	99 (72)[c]
9			**1-Me**		38
10			**1-Ph**		29
11[d]	 **3d**	 **4d**	**1-TPPh**	5	74
12[d]			**1-Me**		10
13[d]			**1-Ph**		5
14[d]	 **3e**	 **4e**	**1-TPPh**	5	88
15[d]			**1-Me**		51
16[d]			**1-Ph**		46

[a] Diolefin (0.25 mmol), catalyst (2.5 μmol, 1.0 mol%), in toluene (5.0 mL), at 0 °C. [b] Yield of **4** based on the GC internal standard technique. [c] Isolated yield. [d] In CH_2Cl_2 (5.0 mL) as the solvent.

that of **1-O-Me** (1.981(5) Å),[4b] implying the TPPh moieties do not obstruct the metal center. **1-Ph** was also prepared similarly.[10]

The RCM of diolefins (**3**) was carried out in toluene or CH_2Cl_2 at 0 °C with the catalyst (1.0 mol%) listed in Fig. 1 (Table 1). Diethyl 2,2-diallylmalonate (**3a**) afforded the corresponding cyclic olefin (**4a**) in 91% yield with **1-TPPh** as catalyst (entry 1). However, the Grubbs second-generation catalyst (**1-Me**) and **1-Ph**, having simple Ph substituent in place of TPPh, provided **4a** in considerably lower yields, 60% and 57%, respectively (entries 2 and 3). The phosphine-free catalyst **1-O-TPPh** was not so effective as **1-TPPh** possibly due to low lability of intramolecular coordination of the isopropoxy unit at such lower temperature (entry 4).[11] The efficacy of **1-TPPh** as compared with **1-Me** and **1-Ph** was also confirmed using various diolefins. In the reaction of malonate esters (**3b** and **3c**) affording six- (**4b**) and seven- (**4c**) membered rings, **1-TPPh** provided the products in much higher yields (entries 5 and 8) than **1-Me** (entries 6 and 9) and **1-Ph** (entries 7 and 10). Furthermore, with **1-TPPh** as the catalyst, diallyl ether (**3d**) and 1,7-octadiene (**3e**) afforded the products (**4d** and **4e**) in 74% and 88% yields (entries 11 and 14), respectively, while **1-Me** (entries 12 and 15) and **1-Ph** (entries 13 and 16) were less efficient. In Table 1, selectivities of the products (**4**) were high, and cross metathesis dimerization/oligomerization did not substantially occur.

Table 2 Effect of added PCy_3 on the ring-closing metathesis of **3a**[a]

Entry	Added PCy_3 (mol%)	Catalyst	Yield of **4a** (%)[b]
1	0.10	**1-TPPh**	94
2	0.10	**1-Me**	38
3	0.20	**1-TPPh**	39
4	0.20	**1-Me**	31

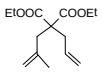
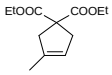
[a] **3a** (0.25 mmol), catalyst (2.5 μmol, 1.0 mol%), added PCy_3 (0.25 μmol: 0.10 mol% or 0.50 μmol, 0.20 mol%), in toluene (5.0 mL), at 0 °C for 17 h. [b] Yield of the product based on the GC internal standard technique.

When 0.10 mol% of PCy_3 was added to entry 1 in Table 1 (where 1.0 mol% of **1-TPPh** was employed as catalyst), the catalyst was still active to provide **4a** in 94% yield (entry 1, Table 2). In sharp contrast, the addition of the same amount (0.10 mol%) of PCy_3 to entry 2 in Table 1 (employing 1.0 mol% of **1-Me**), the catalytic activity significantly decreased and **4a** was afforded in 38% yield (entry 2, Table 2). The TPPh moiety on the NHC ligand might suppress re-coordination of PCy_3 more efficiently than **1-Me** and secure the good catalytic activity under these conditions. On the other hand, the addition of the double amount (0.20 mol %) of PCy_3 to the **1-TPPh** catalyst systems resulted in considerable catalyst deactivation providing **4a** in 39% (entry 3) as observed in entry 4. With the larger amount of the added PCy_3, even **1-TPPh** lowered its catalytic activity.

Hence, we tried to remove PCy_3 from the catalyst systems by adding CuCl as a phosphine scavenger[12] (generating ill-characterized CuCl-PCy_3 complex),[12b] although it is known that these catalysts tend to decompose more rapidly in the presence of CuCl. The reaction of **3a** was carried out with **1-TPPh** as catalyst (1.0 mol%) in the presence of CuCl (4.0 mol%) in THF at 0 °C under otherwise the same reaction conditions as entry 1 in Table 1 (entry 1 in Table 3). Even initial reaction rate in the reaction became much higher, the yield (57% yield after 4 h) did not increase at all during next 24 h, indicating catalyst decomposition. Thus, even **1-TPPh** decomposed fairly fast when the PCy_3 was scavenged by CuCl. **1-Me** decomposed much faster under the same reaction conditions and **4a** was obtained only in 10% yield (entry 2).

Therefore, **1-TPPh*** (Fig. 1) having eight methyl substituents on **1-TPPh** was devised and synthesized by the similar method.[10] Unfortunately, good single crystals of **1-TPPh*** could not be obtained. However, DFT optimized structure (by B3LYP/LANL2DZ) clearly indicated the introduced methyl moieties enhance the shielding effect for the Ru coordination sphere (Fig. S4).[10] In the reaction of **3a** as a substrate, **1-TPPh*** (entry 3) was more efficient catalyst than **1-TPPh** (entry 4) to afford **4a** in 91% yield[13] in 15 min at 10 °C in the presence of CuCl (4.0 mol %) in THF. When the catalyst loading was lowered to 0.04 mol%, the turnover number (TON) reached 12,000 (entry 5). With more sterically congested **3f**, **1-TPPh*** was a superior catalyst and provided **4f** in 90% yield in 15 min (entry 6), while **1-TPPh** and **1-Me** were not effective giving **4f** in 30% and 29% yields, respectively (entries 7 and 8). These yields in entries 6 and 7 did not increase at all even after 4 h, indicating both the catalysts decomposed within a few minutes under these reaction conditions (Fig. S4).[10] **1-TPPh*** was also better catalyst for **3b** and **3c** as the substrates (entries 9 and 12) as compared

Table 3 The ring-closing metathesis of various diolefins in the presence of CuCl in THF[a]

Entry	Diolefin	Product	Catalyst	Temp[b] (°C)	Time (min)	Yield (%)[c]
1[d]	**3a**	**4a**	**1-TPPh**	0	240	57
2[d]			**1-Me**	0	240	10
3			**1-TPPh***	10	15	91 (84)[e]
4			**1-TPPh**	10	15	63
5[f]			**1-TPPh***	RT	60	49
6			**1-TPPh***	RT	15	90 (80)[e]
7			**1-TPPh**			30
8	**3f**	**4f**	**1-Me**			29
9	**3b**	**4b**	**1-TPPh***	0	10	(95)[e]
10			**1-TPPh**			75
11			**1-Me**			33
12	**3c**	**4c**	**1-TPPh***	0	10	94 (88)[e]
13			**1-TPPh**			87
14			**1-Me**			30
15			**1-TPPh***	RT	2	99 (77)[e]
16	**3g**	**4g**	**1-TPPh**			94
17			**1-Me**			33
18			**1-TPPh***	0	10	83 (81)[e]
19	**3h**	**4h**	**1-TPPh**			79
20			**1-Me**			42

[a] Diolefin (0.25 mmol), catalyst (2.5 μmol, 1.0 mol%), CuCl (0.010 mmol: 4.0 mol%), THF (2.0 mL). [b] RT = room temperature. [c] Yield of the product based on the GC internal standard technique. [d] THF (5.0 mL) was used. [e] Isolated yield. [f] **3a** (2.5 mmol), **1-TPPh*** (0.10 μmol, 0.040 mol%), CuCl (1.0 μmol, 0.40 mol%) in THF (0.4 mL) at RT for 60 min.

with **1-TPPh** (entries 10 and 13) and **1-Me** (entries 11 and 14). In the reaction of an allyl ether (**3g**) and a sulfonamide (**3h**), both **1-TPPh*** (entries 15 and 18) and **1-TPPh** (entries 16 and 19) showed higher catalytic activity than **1-Me** (entries 17 and 20). It is noteworthy that in the presence of CuCl, THF plays an important role. When the reaction of entry 3 in Table 3 was carried out in toluene under otherwise identical reaction conditions, yield of **4a** was reduced significantly to 44%.[10] Upon addition of a small amount of THF (0.2 mL) to toluene (1.8 mL) as solvent, the yield of **4a** was recovered to 69%. Coordination of THF to stabilize the catalyst center must be important. THF to stabilize the catalyst center must be important.

In conclusion, ruthenium-based metathesis catalysts with a NHC ligand bearing TPPh and TPPh* moieties (**1-TPPh** and **1-TPPh***) were synthesized. A combination of **1-TPPh*** and CuCl as a phosphine scavenger in THF provides much higher catalytic activity. Further studies on application of the present catalytic system are currently under investigation.

This work was supported by Grant-in-Aid for Scientific Research on Innovative Areas ("Organic synthesis based on reaction integration" and "Molecular activation directed toward straightforward synthesis") from MEXT, Japan.

Notes and references

Department of Energy and Hydrocarbon Chemistry, Graduate School of Engineering, Kyoto University, Kyoto 615-8510, Japan, Fax: +81-75-383-2516; Tel: +81-75-383-2514; E-mail: ytsuji@scl.kyoto-u.ac.jp

† Electronic Supplementary Information (ESI) available: See DOI: 10.1039/b000000x/

‡ Crystallographic data of **1-O-TPPh**: $C_{92}H_{80}Cl_8N_2ORu$, M = 1614.35, triclinic, space group $P\bar{1}$ (No. 2), a = 12.7107(2), b = 14.1983(1), c = 24.5773(13) Å, α = 86.648(8), β = 89.389(8), γ = 63.635(6) °, V = 3471.3(3) Å^3, Z = 2, 16946 independent reflections (R_{int} = 0.065), $R1(I > 2\sigma(I))$ = 0.0857, $wR2$ (all data) = 0.1643. GOF = 1.321. CCDC 82559.

1 (*a*) S.-Y. Hau and S. Chang, in *Handbook of Metathesis*, ed. R. H. Grubbs, Wiley-VHC, Weinheim, 2003, vol. 2, pp. 5; (*b*) R. H. Grubbs and T. M. Trink, in *Ruthenium in Organic Synthesis*, ed. S.-i Murahash, Wiley-VHC, Weinheim, 2004, pp. 153.

2 (*a*) M. Scholl, S. Ding, C. W. Lee and R. H. Grubbs, *Org. Lett.*, 1999, **1**, 953; (*b*) T. M. Trnka and R. H. Grubbs, *Acc. Chem. Res.*, 2001, **34**, 18; (*c*) P. Schwab, M. B. France, J. W. Ziller and R. H. Grubbs, *Angew. Chem. Int. Ed.*, 1995, **34**, 2039; (*d*) P. Schwab, R. H. Grubbs, and J. W. Ziller, *J. Am. Chem. Soc.*, 1996, **118**, 100.

3 (*a*) E. L. Dias, S. T. Nguyen and R. H. Grubbs, *J. Am. Chem. Soc.*, 1997, **119**, 3887; (*b*) M. S. Sanford, L. M. Henling, M. W. Day and R. H. Grubbs, *Angew. Chem. Int. Ed.*, 2000, **39**, 3451; (*c*) M. S. Sanford, M. Ulman and R. H. Grubbs, *J. Am. Chem. Soc.*, 2001, **123**, 749; (*d*) M. S. Sanford, J. A. Love and R. H. Grubbs, *J. Am. Chem. Soc.*, 2001, **123**, 6543; (*e*) J. A. Love, M. S. Sanford, M. W. Day and R. H. Grubbs, *J. Am. Chem. Soc.*, 2003, **125**, 10103.

4 (*a*) J. A. Love, J. P. Morgan, T. M. Trnka and R. H. Grubbs, *Angew. Chem. Int. Ed.*, 2002, **41**, 4035; (*b*) M. S. Sanford and J. A. Love in *Handbook of Metathesis*, ed. R. H. Grubbs, Wiley-VHC, Weinheim, 2003, vol. 1, pp. 129; (*c*) S. B. Garber, J. S. Kingsbury, B. L. Gray and A. H. Hoveyda, *J. Am. Chem. Soc.*, 2000, **122**, 8168; (*d*) H. Wakamatsu and S. Blechert, *Angew. Chem. Int. Ed.*, 2002, **41**, 749; (*e*) H. Wakamatsu and S. Blechert, *Angew. Chem. Int. Ed.*, 2002, **41**, 2403; (*f*) F. Boeda, H. Clavier and S. P. Nolan, *Chem. Commun.*, 2008, 2726; (*g*) A. Michrowska, R. Bujok, A. Harutyunyan, V. Sashuk, G. Dolgonos and K. Grrela, *J. Am. Chem. Soc.*, 2004, **126**, 9318.

5 (*a*) C. Samojlowicz, M. Bieniek and K. Grela, *Chem. Rev.*, 2009, **109**, 3708, and references sited therein; (*b*) K. M. Kuhn, J.-B. Bourg, C. K. Chung, S. C. Virgil and R. H. Grubbs, *J. Am. Chem. Soc.*, 2009, **131**, 5313; (*c*) L. Vieille-Petit, H. Clavier, A. Linden, S. Blumentritt, S. P. Nolan and R. Dorta, *Organometallics*, 2010, **29**, 775; (*d*) M. Gatti, L. Vieille-Petit, X. Luan, R. Mariz, E. Drinkel, A. Linden and R. Dorta, *J. Am. Chem. Soc.*, 2009, **131**, 9498.

6 (*a*) T. Fujihara, K. Semba, J. Terao and Y. Tsuji, *Angew. Chem. Int. Ed.*, 2010, **49**, 1472; (*b*) H. Ohta, M. Tokunaga, Y. Obora, T. Iwai, T. Iwasawa, T. Fujihara and Y. Tsuji, *Org. Lett.*, 2007, **9**, 89; (*c*) O. Niyomura, M. Tokunaga, Y. Obora, T. Iwasawa and Y. Tsuji, *Angew. Chem. Int. Ed.*, 2003, **42**, 1287.

7 (*a*) T. Fujihara, S. Yoshida, H. Ohta and Y. Tsuji, *Angew. Chem. Int. Ed.*, 2008, **47**, 8310; (*b*) T. Fujihara, S. Yoshida, J. Terao and Y. Tsuji, *Org. Lett.*, 2009, **11**, 2121.

8 (*a*) T. Iwasawa, M. Tokunaga, Y. Obora and Y. Tsuji, *J. Am. Chem. Soc.*, 2004, **126**, 6554; (*b*) H. Aoyama, M. Tokunaga, J. Kiyosu, T. Iwasawa, Y. Obora and Y. Tsuji, *J. Am. Chem. Soc.*, 2005, **127**, 10474.

9 (*a*) S. H. Hong, A. G. Wenzel, T. T. Salguero, M. W. Day and R. H. Grubbs, *J. Am. Chem. Soc.*, 2007, **129**, 7961; (*b*) S. H. Hong, M. W. Day and R. H. Grubbs, *J. Am. Chem. Soc.*, 2004, **126**, 7414.

10 See ESI for detail.

11 T. Vorfalt, K.-J. Wannowius and H. Plenio, *Angew. Chem. Int. Ed.*, 2010, **49**, 5533.

12 (*a*) E. L. Dias, S. T. Nguyen and R. H. Grubbs, *J. Am. Chem. Soc.*, 1997, **119**, 3887; (*b*) E. L. Dias and R. H. Grubbs, *Organometallics*, 1998, **17**, 2758; (*c*) M. Ulman and R. H. Grubbs, *J. Org. Chem.*, 1999, **64**, 7202.

13 When **1-TPPh*** was used as a catalyst in entry 1 in Table 1 under otherwise identical conditions , **4a** was obtained in 91% yield after 24 h.